



West Middlesex University Hospital

Taxol (Paclitaxel) in Pregnancy

Date of Search: 10/08/2016

Sources: Medline, Embase.

Search History:

1. EMBASE; taxol.ti; 2602 results.
2. EMBASE; Paclitaxel.ti; 15503 results.
3. EMBASE; *PACLITAXEL/; 21744 results.
4. EMBASE; 1 OR 2 OR 3; 23768 results.
5. EMBASE; pregn*.ti; 227043 results.
6. EMBASE; exp PREGNANCY/; 624507 results.
7. EMBASE; 5 OR 6; 669424 results.
8. EMBASE; 4 AND 7; 51 results.
9. Medline; taxol.ti; 1918 results.
10. Medline; Paclitaxel.ti; 10478 results.
11. Medline; *PACLITAXEL/; 11137 results.
12. Medline; 9 OR 10 OR 11; 15146 results.
13. Medline; pregn*.ti; 182126 results.
14. Medline; exp PREGNANCY/; 790732 results.
15. Medline; 13 OR 14; 806123 results.
16. Medline; 12 AND 15; 51 results.
17. Medline; exp MATERNAL-FETAL EXCHANGE/; 28250 results.
18. Medline; 12 AND 17; 2 results.
19. Medline; exp FETUS/; 146233 results.
20. Medline; 12 AND 19; 15 results.
21. EMBASE; exp PRENATAL DRUG EXPOSURE/; 8374 results.
22. EMBASE; 4 AND 21; 1 results.
23. EMBASE; exp PREGNANCY OUTCOME/; 40008 results.
24. EMBASE; 4 AND 23; 6 results.
25. EMBASE; exp TERATOGENICITY/; 15259 results.
26. EMBASE; 4 AND 25; 5 results.
27. EMBASE; exp TERATOGENESIS/; 7969 results.
28. EMBASE; 4 AND 27; 1 results.
29. Medline; exp TERATOGENESIS/ OR exp TERATOGENS/; 25130 results.
30. Medline; 12 AND 29; 28 results.
31. Medline; taxane*.ti; 1672 results.
32. Medline; exp PACLITAXEL/; 21599 results.
33. Medline; 15 AND 31 AND 32; 2 results.
34. Medline; 17 AND 31 AND 32; 1 results.
35. EMBASE; taxane*.ti; 2784 results.

36. EMBASE; exp PACLITAXEL/; 80748 results.
37. EMBASE; 7 AND 35 AND 36; 10 results.
38. EMBASE; 21 AND 35 AND 36; 1 results.
39. EMBASE; 23 AND 35 AND 36 AND 37; 1 results.
40. EMBASE; 25 AND 35 AND 36; 0 results.
41. EMBASE; 27 AND 35 AND 36; 0 results.

Title: Chemotherapy and pregnancy: Effects of taxanes exposure on placental drug transporters expression

Citation: American Journal of Obstetrics and Gynecology, January 2015, vol./is. 212/1 SUPPL. 1(S265), 0002-9378 (January 2015)

Author(s): Berveiller P., Degrelle S., Segond N., Tsatsaris V., Selleret L., Mir O., Evain-Brion D., Gil S.

Language: English

Abstract: OBJECTIVE: The use of taxanes in pregnant cancer patients is increasing. Even if recent clinical data are reassuring, little is known about their effects on the placenta itself. Therefore, we aimed in this study to assess the effects of paclitaxel on placental drug transporters expression, using in vitro, ex vivo and in vivo placental models. STUDY DESIGN: First, using human primary trophoblast culture model, trophoblasts were isolated from normal term placentas and subsequently exposed in vitro to paclitaxel. Transcriptional regulation of various drug transporters genes was assessed with RT-qPCR, and protein expression of two famous drug transporters was also studied (P-gp and BCRP). Secondly, placentas from pregnant women treated with paclitaxel during pregnancy were collected. Placental tissue extracts were subsequently analysed in order to assess protein expression of P-gp and BCRP. Finally, placental tissues were isolated after an ex vivo placental perfusion of paclitaxel. Drug transporter regulation was assessed and compared with results obtained from in vivo study. RESULTS: Twelve drug-transporters genes were significantly downregulated after exposure to paclitaxel in primary trophoblast culture. Conversely, no drug transporter gene was found to be significantly up-regulated. Besides, P-gp and BCRP expression was not significantly regulated after paclitaxel administration. Interestingly, P-gp and BCRP protein expression seemed to be significantly increased in placentas from mothers chronically treated with paclitaxel during pregnancy vs. ex vivo cotyledons perfused with paclitaxel. CONCLUSION: Our study provided original data, highlighting the potential regulation of paclitaxel on placental drug transporters expression. Moreover, mode of administration of paclitaxel (chronic vs. temporary) might have different consequences. Thus, physicians should take into account that anticancer agents may have repercussions not only via the transplacental transfer, but also via their direct effects on the placenta itself. (Figure Presented).

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Optimizing anticancer drug treatment in pregnant cancer patients: pharmacokinetic analysis of gestation-induced changes for doxorubicin, epirubicin, docetaxel and paclitaxel.

Citation: *Annals of oncology* : official journal of the European Society for Medical Oncology / ESMO, Oct 2014, vol. 25, no. 10, p. 2059-2065, 1569-8041 (October 2014)

Author(s): van Hasselt, J G C, van Calsteren, K, Heyns, L, Han, S, Mhallem Gziri, M, Schellens, J H M, Beijnen, J H, Huitema, A D R, Amant, F

Abstract: Pregnant patients with cancer are increasingly treated with anticancer drugs, although the specific impact of pregnancy-induced physiological changes on the pharmacokinetics (PK) of anticancer drugs and associated implications for optimal dose regimens remains unclear. Our objectives were to quantify changes in PK during pregnancy for four frequently used anticancer agents doxorubicin, epirubicin, docetaxel and paclitaxel, and to determine associated necessary dose adjustments. A pooled analysis of PK data was carried out for pregnant (Pr) and nonpregnant (NPr) patients for doxorubicin (n = 16 Pr/59 NPr), epirubicin (n = 14 Pr/57 NPr), docetaxel (n = 3 Pr/32 NPr) and paclitaxel (n = 5 Pr/105 NPr). Compartmental nonlinear mixed effect models were used to describe the PK and gestational effects. Subsequently, we derived optimized dose regimens aiming to match to the area under the concentration-time curve (AUC) in nonpregnant patients. The effect of pregnancy on volumes of distribution for doxorubicin, epirubicin, docetaxel and paclitaxel were estimated as fold-change of <1.32, <2.08, <1.37 and <4.21, respectively, with adequate precision [relative standard error (RSE) <37%]. For doxorubicin, no gestational effect could be estimated on clearance (CL). For epirubicin, docetaxel and paclitaxel, a fold-change of 1.1 (RSE 9%), 1.19 (RSE 7%) and 1.92 (RSE 21%) were, respectively, estimated on CL. Calculated dose adjustment requirements for doxorubicin, epirubicin, docetaxel and paclitaxel were +5.5%, +8.0%, +16.9% and +37.8%, respectively. Estimated changes in infusion duration were marginal (<4.2%) except for paclitaxel (-21.4%). Clinicians should be aware of a decrease in drug exposure during pregnancy and should not a priori reduce dose. The decrease in exposure was most apparent for docetaxel and paclitaxel which is supported by known physiological changes during pregnancy. The suggested dose adaptations should only be implemented after conduct of further confirmatory studies of the PK during pregnancy. © The Author 2014. Published by Oxford University Press on behalf of the European Society for Medical Oncology. All rights reserved. For permissions, please email: journals.permissions@oup.com.

Source: Medline

Full Text:

Available from *Highwire Press* in [Annals of Oncology](#)

Available from *Oxford University Press* in [Annals of Oncology](#); Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Drug selection and dosing in pregnant cancer patients: insights from clinical pharmacokinetics.

Citation: *Annals of oncology* : official journal of the European Society for Medical Oncology / ESMO, Oct 2014, vol. 25, no. 10, p. 1869-1870, 1569-8041 (October 2014)

Author(s): Berveiller, P, Selleret, L, Mir, O

Source: Medline

Full Text:

Available from *Highwire Press* in [Annals of Oncology](#)

Available from *Oxford University Press* in [Annals of Oncology](#); Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Pharmacokinetics, placenta, and brain uptake of paclitaxel in pregnant rats.

Citation: *Cancer chemotherapy and pharmacology*, May 2014, vol. 73, no. 5, p. 1041-1045, 1432-0843 (May 2014)

Author(s): Lee, Na-Young, Lee, Kyung-Bok, Kang, Young-Sook

Abstract: Today, cancer incidence during pregnancy is increasing as women delay childbearing until later in life. Therefore, chemotherapy is regularly administered in pregnant women with cancer. In the present study, we evaluated the change in the pharmacokinetics and the fetus distribution of paclitaxel during pregnancy using pregnant rats. Pharmacokinetic parameters, placenta, and brain transport of [(3)H]paclitaxel were investigated in nonpregnant or pregnant rats using single intravenous injection technique. The plasma pharmacokinetics of paclitaxel in pregnant rats was markedly different compared with nonpregnant rats. The V_{dss} and CL of paclitaxel in pregnant rats were increased, and AUC was decreased compared with nonpregnant rats. The fetus uptake of paclitaxel is markedly lower than the placenta uptake. Paclitaxel is a substrate of P-glycoprotein (P-gp), so P-gp would affect the transport of paclitaxel to the fetus. The brain uptake of [(3)H]paclitaxel was about two fold lower than that of nonpregnant rats. Current findings are important when considering cancer treatment with paclitaxel during pregnancy.

Source: Medline

Full Text:

Available from *Springer Link Journals* in [Cancer Chemotherapy and Pharmacology](#)

Available from *ProQuest* in [Cancer Chemotherapy and Pharmacology](#)

Title: Taxanes for Breast Cancer during Pregnancy: A Systematic Review

Citation: Clinical Breast Cancer, February 2013, vol./is. 13/1(16-23), 1526-8209;1938-0666 (February 2013)

Author(s): Zagouri F., Sergentanis T.N., Chrysikos D., Dimitrakakis C., Tsigginou A., Zografos C.G., Dimopoulos M.-A., Papadimitriou C.A.

Language: English

Abstract: Landmark studies have established taxanes in the treatment of patients with breast cancer; however, recommendations regarding their administration during pregnancy are controversial. The present systematic review aims to synthesize all available data that stem exclusively from breast cancer case series to evaluate the efficacy and safety of taxanes during pregnancy. Overall, 16 studies (50 pregnancies) were eligible for the systematic review according to prisma guidelines. The mean age of patients with breast cancer at pregnancy was 34.6 years. The gestational age (GA) at chemotherapy administration varied from 12 to 36 weeks. The mean GA at delivery was 35.9 weeks. The mean weight of babies at delivery was 2380 g. In 76.7% of cases, a completely healthy neonate was born; in the remaining cases, a neonate who was dystrophic and premature, one with mild hydrocephalus, one with signs of bacterial sepsis, one with hyperbilirubinemia, one with apnea of prematurity, respiratory distress syndrome and gastroesophageal reflux, one with meconium-stained fluid, and another neonate with neutropenia and pyloric stenosis were reported. Ninety percent of children were completely healthy, with a median follow-up of 16 months; in the remaining cases, one child with recurrent otitis media, one with immunoglobulin A deficiency and mild constipation, and another child with delayed speech were reported. In conclusion, available data suggest that taxanes may potentially play a promising role in the optimal therapeutic strategy of patients with breast cancer diagnosed during pregnancy. © 2013 Elsevier Inc.

Publication Type: Journal: Review

Source: EMBASE

Title: Study of transplacental transfer of taxanes using the human ex vivo perfused cotyledon model

Citation: Fundamental and Clinical Pharmacology, June 2013, vol./is. 27/(109), 0767-3981 (June 2013)

Author(s): Vinot C., Giraud C., Rezai K., Peytavin G., Urien S., Gavard L., Mandelbrot L., Treluyer J.M.

Language: English

Abstract: Objective: Taxanes, namely docetaxel and paclitaxel are used without distinction in pregnant women to treat breast cancer during pregnancy. The aim of the present study was to compare the transplacental transfer of these two drugs by using the human placental

perfusion model to help guiding clinicians to choose the safer treatment. Materiel and Methods: Term placentas were obtained from uncomplicated vaginal or caesarean deliveries. They were perfused during 180 min with paclitaxel or docetaxel and physiological albumin concentrations in a recirculating closed configuration. Taxane transfer from the maternal to fetal compartment was calculated according to the following equation: $\%transfer = (Cf \cdot Vf) \cdot 100 / [(Cf \cdot Vf) + (Cm \cdot Vm)]$ where Cf is the drug concentration in the fetal perfusate, Vf the volume of fetal perfusate, Cm the drug concentration in maternal perfusate, and Vm the volume of maternal perfusate. Then, the data were analyzed using a non linear mixed effects model to estimate the maximal drug transfer. Results: Sixteen placentas were perfused, eight with paclitaxel and eight with docetaxel. The placental transfer of paclitaxel at the end of the perfusion was significantly higher than that of docetaxel [38.7 +/- 11.4% vs. 28.1 +/- 10.4%; $P < 10^{-4}$ (mean +/- SD)]. The maximal drug percentage transfer value of paclitaxel was also higher than that of docetaxel (57.7 +/- 6.4 vs. 34.2 +/- 4.3%; $P < 10^{-4}$ (estimate +/- SE). Conclusion: In the present work, we report original data on placental taxane transfer using an ex vivo human perfusion model. The recirculating closed configuration was chosen to reproduce the physiological conditions during the third trimester of pregnancy. However, these results would need to be supported by in vivo data obtained from paired maternal and cord blood samples.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Available from *John Wiley and Sons* in [Fundamental and Clinical Pharmacology](#)
Available from *John Wiley and Sons* in [Fundamental and Clinical Pharmacology](#)

Title: Maternal and fetal outcomes of taxane chemotherapy in breast and ovarian cancer during pregnancy: case series and review of the literature.

Citation: Annals of oncology : official journal of the European Society for Medical Oncology / ESMO, Dec 2012, vol. 23, no. 12, p. 3016-3023, 1569-8041 (December 2012)

Author(s): Cardonick, E, Bhat, A, Gilmandyar, D, Somer, R

Abstract: The purpose of this study was to evaluate the use of taxane chemotherapy during pregnancy and compare maternal and neonatal outcomes with those in women who did not receive taxanes during pregnancy, and review current existing data. This is a retrospective cohort study in which women were identified from the Cancer and Pregnancy Registry at Robert Wood Johnson Medical Center. A retrospective chart analysis and an independent t-test were carried out comparing patient outcomes. A literature search in Ovid, Medline and PubMed was then carried out using the terms 'breast or ovarian cancer', 'pregnancy', 'paclitaxel', 'docetaxel', 'taxanes' and 'chemotherapy'. Twelve of 129 women with breast cancer were exposed to taxanes during pregnancy. Three of nine women with ovarian cancer received taxane-based treatment during pregnancy. Birth weight, gestational age at delivery, rate of growth restriction, congenital anomalies and incidence of maternal and neonatal neutropenia were not statistically different between the two groups. Taxane-

based chemotherapy does not appear to increase the risk of fetal or maternal complications when compared with conventional chemotherapy in the small cohort of women in our Registry.

Source: Medline

Full Text:

Available from *Highwire Press* in [Annals of Oncology](#)

Available from *Oxford University Press* in [Annals of Oncology](#); Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Maternal and neonatal outcomes of dose-dense chemotherapy for breast cancer in pregnancy

Citation: *Obstetrics and Gynecology*, December 2012, vol./is. 120/6(1267-1272), 0029-7844 (December 2012)

Author(s): Cardonick E., Gilmandyar D., Somer R.A.

Language: English

Abstract: OBJECTIVE: To estimate the effect of dose-dense chemotherapy during pregnancy on maternal and neonatal outcomes. METHODS: This is a retrospective cohort study in which women were identified from the international Cancer and Pregnancy Registry at Cooper Medical School at Rowan University in Camden, New Jersey. A chart analysis was completed and Fisher's exact test and independent t test were used in comparing patient outcomes. RESULTS: Ten women received dose-dense chemotherapy, received every 2 weeks, and 99 women received conventional chemotherapy, received with at least 3-week intervals, for breast cancer during pregnancy. Birth weight, gestational age at delivery, rate of growth restriction, congenital anomalies, and incidence of maternal and neonatal neutropenia were not statistically different between the two groups. CONCLUSION: In the small cohort of women in our registry, dose-dense chemotherapy does not appear to increase the risk of fetal or maternal complications. © 2012 by The American College of Obstetricians and Gynecologists.

Publication Type: Journal: Article

Source: EMBASE

Full Text:

Available from *Obstetrics and Gynecology* in [Patricia Bowen Library and Knowledge Service West Middlesex university Hospital](#)

Available from *Ovid* in [Obstetrics and Gynecology](#)

Available from *Ovid* in [Obstetrics and gynecology.](#)

Title: Comparative transplacental transfer of taxanes using the human perfused cotyledon placental model.

Citation: American journal of obstetrics and gynecology, Dec 2012, vol. 207, no. 6, p. 514.e1, 1097-6868 (December 2012)

Author(s): Berveiller, Paul, Vinot, Cécile, Mir, Olivier, Broutin, Sophie, Deroussent, Alain, Seck, Atmane, Camps, Sandra, Paci, Angelo, Gil, Sophie, Tréluyer, Jean-Marc

Abstract: The use of taxanes (paclitaxel and docetaxel) in pregnant cancer patients is increasing. We aimed to compare their transplacental transfer using the gold standard human placental perfusion model, to guide drug selection. Term placentas were perfused with paclitaxel or docetaxel and 2 different albumin concentrations. Main transfer parameters such as fetal transfer rate (FTR), clearance index, and placental uptake of taxanes were assessed. Twelve placentas were perfused, 6 with paclitaxel and 6 with docetaxel. Mean FTR of paclitaxel decreased significantly from $5.67 \pm 0.02\%$ in low albumin conditions to $1.72 \pm 0.09\%$ in physiological albumin conditions. Similarly, mean clearance index decreased significantly from 0.22 ± 0.02 to 0.09 ± 0.01 . Regarding docetaxel, mean FTR were similar in low albumin and physiological conditions ($5.03 \pm 0.60\%$ and $4.04 \pm 0.22\%$, respectively) while mean clearance index decreased significantly from 0.18 ± 0.02 to 0.13 ± 0.01 . Taxanes accumulation in cotyledon was similar for docetaxel and paclitaxel: $4.54 \pm 1.84\%$ vs $3.31 \pm 1.88\%$, respectively. Transplacental transfer and placental accumulation of paclitaxel and docetaxel were low and similar, especially in physiological conditions of albumin. Further studies are warranted to optimize the selection of a taxane in pregnant cancer patients. Copyright © 2012 Mosby, Inc. All rights reserved.

Source: Medline

Title: Cancer chemotherapeutic agents as human teratogens

Citation: Birth Defects Research Part A - Clinical and Molecular Teratology, August 2012, vol./is. 94/8(626-650), 1542-0752;1542-0760 (August 2012)

Author(s): Selig B.P., Furr J.R., Huey R.W., Moran C., Alluri V.N., Medders G.R., Mumm C.D., Hallford H.G., Mulvihill J.J.

Language: English

Abstract: BACKGROUND: Cancer is the second leading cause of death among women of reproductive age. Although the coincidence of pregnancy and cancer is rare and treatment may sometimes be safely delayed, the use of chemotherapeutic agents in pregnancy is sometimes unavoidable or inadvertent. METHODS: We review the literature for the use of antineoplastic agents in single-agent and combination therapy from 1951 through June 2012. We also summarize the evidence relating to teratogenicity of disorder-specific combination chemotherapy treatments for those malignancies frequently encountered in

women of childbearing age. Major endpoints were called "adverse pregnancy outcomes" (APOs), to include structural anomalies (congenital malformations), functional defects, blood or electrolyte abnormalities, stillbirths, spontaneous abortions (miscarriages), and fetal, neonatal, or maternal deaths. RESULTS: The registry totals 863 cases. Rates of APOs (and congenital malformations) after any exposure were 33% (16%), 27% (8%), and 25% (6%), for first, second, and third trimesters. Among the groups of cancer drugs, antimetabolites and alkylating agents have the highest rates of APOs. Mitotic inhibitors and antibiotics seem more benign. Mixed results were observed from single-agent exposure, often because of small numbers of exposures. As a whole, the alkylating agents and antimetabolites are more harmful when given as a single agent rather than as part of a regimen. First-trimester exposure poses a more permanent risk to the fetus. CONCLUSIONS: Systematic ascertainment of women early in pregnancy, preferably in a population base, is needed for assessment of true risks. Long-term follow-up is needed to rule out neurobehavioral effects. Birth Defects Research (Part A) 94:626-650, 2012. © 2012 Wiley Periodicals, Inc..

Publication Type: Journal: Review

Source: EMBASE

Full Text:

Available from *John Wiley and Sons* in [Birth Defects Research Part A: Clinical and Molecular Teratology](#)

Title: Oligohydramnios associated with administration of weekly paclitaxel for triple-negative breast cancer during pregnancy

Citation: Annals of Oncology, September 2011, vol./is. 22/9(2151-2152), 0923-7534;1569-8041 (September 2011)

Author(s): Shieh M.P., Mehta R.S.

Language: English

Publication Type: Journal: Letter

Source: EMBASE

Full Text:

Available from *Highwire Press* in [Annals of Oncology](#)

Available from *Oxford University Press* in [Annals of Oncology](#); Note: ; Collection notes: To access please select Login with Athens and search and select NHS England as your institution before entering your NHS OpenAthens account details.

Title: Taxanes for treatment of cancer occurring during pregnancy: Study of placental transfers of paclitaxel and docetaxel with the ex vivo perfused human cotyledon model

Citation: Fundamental and Clinical Pharmacology, April 2011, vol./is. 25/(36), 0767-3981 (April 2011)

Author(s): Berveiller P., Gil S., Mir O., Vinot C., Urien S., Chissey A., Simasotchi C., Tsatsaris V., Treluyer J.

Language: English

Abstract: Introduction: In France, the occurrence of cancer during pregnancy averages 700 women annually, with breast cancer being the most frequent malignancy. Chemotherapy may be indicated in some patients, leaving questionable the transplacental transfer of anticancer drugs, especially emerging molecules in breast cancer treatment such as taxanes. The aim of this study was to compare the transplacental transfer of paclitaxel and docetaxel, using the perfused placental lobule model, the gold standard ex vivo method. Methods: Placentas were obtained from uncomplicated full-term pregnancies and were collected immediately after delivery. Cotyledons were perfused with paclitaxel or docetaxel in different experimental conditions according to the modified method described by Schneider et al. Maternal perfusion comprised antipyrine 20 mg/L as internal control. Maximal concentrations (1500 and 4000 ng/mL for paclitaxel and docetaxel, respectively) as well as twofold increased concentrations were tested. Main transfer parameters as Fetal Transfer Rate (FTR, corresponding to the ratio of fetal to maternal concentrations) and Clearance Index (CI corresponding to the ratio of paclitaxel or docetaxel FTR to antipyrine FTR) of paclitaxel and docetaxel were assessed. Paclitaxel, docetaxel and antipyrine concentrations were determined by High-Performance Liquid Chromatography (HPLC). Results: Seven placental lobules were perfused with paclitaxel (1272-1598 ng/ mL) and docetaxel (3708-4227 ng/mL). Maximal foetal concentrations were 153 and 472 ng/mL for paclitaxel and docetaxel respectively. Mean FTR were 3.85 +/- 2% and 5.5 +/- 2.2% for paclitaxel and docetaxel, respectively. Mean CI of paclitaxel and docetaxel were 0.16 +/- 0.09 and 0.18 +/- 0.05, respectively with a difference being not statistically significant (P = 0.326). These data suggest that both drugs cross the placenta at a relatively low rate. Conclusion: The placental transfer of paclitaxel and docetaxel, two highly proteinbound molecules, were compatible with passive diffusion of the unbound fraction. In this study, transplacental transfers of paclitaxel and docetaxel were similar and relatively limited at Cmax and with a low albumin concentration. These original results seemed to confirm reassuring retrospective clinical data which did not show any significant difference in terms of foetal morbidity between paclitaxel and docetaxel.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Available from *John Wiley and Sons* in [Fundamental and Clinical Pharmacology](#)

Available from *John Wiley and Sons* in [Fundamental and Clinical Pharmacology](#)

Title: Transplacental transfer of paclitaxel, docetaxel, carboplatin, and trastuzumab in a baboon model

Citation: International journal of gynecological cancer : official journal of the International Gynecological Cancer Society, December 2010, vol./is. 20/9(1456-1464), 1525-1438 (Dec 2010)

Author(s): Calsteren K.V., Verbesselt R., Devlieger R., De Catte L., Chai D.C., Van Bree R., Heyns L., Beijnen J., Demarsin S., de Bruijn E., de Hoon J., Amant F.

Language: English

Abstract: The paucity of data on fetal effects of prenatal exposure to chemotherapy prompted us to study the transplacental transport of commonly used anticancer agents in a pregnant baboon model. Single or combination chemotherapy with paclitaxel, docetaxel, carboplatin, and trastuzumab was administered to 9 baboons at a mean (SD) gestational age of 117 (26) days (paclitaxel, 100 mg/m² [n = 2]; docetaxel, 100 mg/m² [n = 2]; paclitaxel, 175 mg/m² with carboplatin, area under the curve of 6 at standard dosage [n = 2] and 50% dosage [n = 1]; docetaxel, 75 mg/m² with carboplatin, area under the curve 6 [n = 1]; and docetaxel, 75 mg/m² with trastuzumab, 8 mg/kg [n = 1]). Serial fetal and maternal blood samples, amniotic fluid, maternal urine, and fetal and maternal tissue samples were collected for the first 76 hours after drug infusion. Levels of carboplatin were determined by atomic absorption spectrometry, docetaxel and paclitaxel by high-performance liquid chromatography, and trastuzumab by enzyme-linked immunosorbent assay. Fetal plasma concentrations of carboplatin averaged 57.5% (14.2%) of maternal concentrations (n = 7). Fetal plasma concentrations were 1.5% (0.8%) of maternal concentrations (n = 7). Immediately after ending the infusion, paclitaxel was not detectable in fetal tissues, whereas, after 3 hours, fetal tissues contained 15% of maternal tissue concentrations. Docetaxel could not be detected in fetal blood samples (n = 9). In the first 3 hours after docetaxel infusion, fetal tissues contained 5.0% to 50.0% of maternal tissue concentrations, whereas equal fetal and maternal tissue concentrations were found after 26 and 76 hours. The transplacental passages of trastuzumab were 85.0% and 3.0%, 2 and 26 hours after trastuzumab infusion, respectively. After 26 hours, amniotic fluid contained 36.4% of the fetal plasma concentration. Fetal tissue concentrations varied between 5.0% and 14.0% of the maternal concentration. Variable plasma and/or tissue concentrations of taxanes, carboplatin, and trastuzumab were encountered in the fetal compartment. These data are important when cancer treatment is considered during pregnancy and underline the need for long-term follow-up of children after prenatal exposure to these cytotoxic agents.

Publication Type: Journal: Article

Source: EMBASE

Full Text:

Available from *Ovid* in [International Journal of Gynecological Cancer](#)

DISCLAIMER: Results of database and or Internet searches are subject to the limitations of both the database(s) searched, and by your search request. It is the responsibility of the requestor to determine the accuracy, validity and interpretation of the results.
